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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,454	01/14/2002	Guido Grandi	PP01591.101	4170

7590

04/29/2005

Alisa A Harbin  
Chiron Corporation  
Intellectual Property R-338  
P O Box 8097  
Emeryville, CA 94662-8097

EXAMINER

MINNIFIELD, NITA M

ART UNIT

PAPER NUMBER

1645

DATE MAILED: 04/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. 09/914,454	Applicant(s) GRANDI ET AL.	
	Examiner N. M. Minnifield	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 24 January 2005.
- 2a) ☐ This action is FINAL.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-21,23-25,27-39 and 43-45 is/are pending in the application.
- 4a) Of the above claim(s) 27-39 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-21,23-25 and 43-45 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 27-39 are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) <u>6 sheets</u>   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>12/16/02</u> <u>4 sheets</u> | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

1. Applicants' amendment filed January 24, 2005 is acknowledged and has been entered. Claims 22, 26 and 40-42 have been canceled. Claims 3, 6, 13-15, 17-20, 32, 34 and 37 have been amended. New claims 43-45 have been added. Claims 1-21, 23-25, 27-39 and 43-45 are pending in the present application.

2. Applicant's election without traverse of January 24, 2005 in the reply filed on Group I, claims 1-21, 23-25, 43-45, and SEQ IDNO: 31 (peptide) and species SEQ ID NO: 1 (oligonucleotide) is acknowledged.

It is noted that the Examiner has considered all of Applicants' comments/arguments, amendment to the claims, the groupings of inventions in the original restriction requirement as well as the proposed regrouping of inventions for the restriction requirement, proposed by Applicant. The Examiner agrees and the groups of inventions in this application are:

Group I, claims 1-21, 23-25 and 43-45, drawn to immunogenic and vaccine compositions.

Group II, claims 27-31, drawn to adjuvant compositions.

Group III, claims 32-39, drawn to methods of inducing immune responses.

Applicants have asserted that an examination of all of the inventions "...would not impose a serious burden on the Examiner. Indeed, applicants believe that failure to examine the claims as proposed would pose a far greater burden on the Patent and Trademark Office, by requiring a duplication of effort and resources, since a search directed to claims in Groups I and II, and similarly Groups IV and V, would turn up overlapping art if such art existed. Accordingly,

applicants respectfully traverse the above Restriction Requirement and request reconsideration thereof.

However, the restriction Groups have acquired a separate status in the art as a separate subject for inventive effect and require independent searches. The search for each of the above inventions is not co-extensive particularly with regard to the literature search. A reference, which would anticipate the invention of one group would not necessarily anticipate or make obvious any of the other groups. Moreover, as to the question of burden of search, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Burden in examining materially different groups having materially different issues (35 U.S.C. 101, 102, 103, and 112) also exist. The restriction requirement is made final.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments, submitted after final rejection, are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104.

Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

The requirement is deemed proper and is made FINAL.

3. Claims 27-39 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on January 24, 2005.

4. The disclosure is objected to because of the following informalities: All of the sequences recited in the specification do not have a sequence identifier as required, see pages 32 and 33. Appropriate correction is required.

5. Claims 9-14 and 43-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are vague and indefinite in the recitation of “oil droplets substantially all of which...”. The metes and bounds of “substantially all” have not been defined. Do all (i.e. 100%) of the oil droplets have to be less than 1 micron in diameter or can the composition have 90% of the oil droplets with a diameter of less than 1 micron?

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(c) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1, 3, 6, 7, 17-21, 23 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Agrawal et al (WO 98/49288).

It is noted that the effective filing date for this application is February 9, 2000. Applicants have claimed priority to provisional application 60/121792 filed February 26, 1999, however this application is not complete. The application does not have any nucleotide or amino acid sequences set forth nor a RSL that is in compliance with the sequence rules. It is not clear that Applicants had possession of the claimed sequences at the time of filing the provisional application 60/121792.

Agrawal et al discloses a composition comprising a Neisseria antigen and a adjuvant composition comprising an oligonucleotide comprising at least one CG motif. The prior art discloses that the compositions can be used for methods for prophylactically protect a mammal from infection by a pathogen (p. 4). Agrawal et al discloses that pathogens include Neisseria spp. (p. 12). Agrawal et al discloses an oligonucleotide that has at least one CG motif and it has at least one phosphorothioate bond (see p. 5; p. 10). Agrawal et al disclose that the CG motif be flanked by two purines immediately 5' to said motif and two pyrimidines immediately 3' to said motif (see p. 11). Agrawal et al disclose that the oligonucleotide should be formulated in a physiologically acceptable carrier or diluent, including without limitation saline and/or an adjuvant (pp. 8-9).

The recitation of vaccine is viewed as intended use. The recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process



of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 370 F.2d 576, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 312 F.2d 937, 939, 136 USPQ 458, 459 (CCPA 1963).

The prior art discloses that claimed invention. Since the Patent Office does not have the facilities for examining and comparing applicants' compositions with the compositions of the prior art reference, the burden is upon applicants to show a distinction between the material structural and functional characteristics of the claimed compositions and the compositions of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594.

11. Claims 1-4, 6-15, 17, 23, 24, 44 and 45 are rejected under 35 U.S.C. 102(a) as being anticipated by Ruelle et al (WO 99/58683).

Ruelle et al disclose a composition comprising a Neisseria antigen and a immunostimulatory oligonucleotide (abstract; p. 4; pp. 31-33). Ruelle et al discloses that the composition may also include an adjuvant (oil-in-water emulsion, aluminum phosphate, aluminum hydroxide) (pp. 34-37). The oil-in-water emulsions comprise metabolisable oil such as squalene. Ruelle et al discloses that the emulsion comprises 2 to 10% oil (squalene) and 0.3 to 3% Tween 80 which is an emulsifying agent (p. 37).

The recitation of vaccine is viewed as intended use. The recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process

of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 370 F.2d 576, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 312 F.2d 937, 939, 136 USPQ 458, 459 (CCPA 1963).

The prior art discloses that claimed invention. Since the Patent Office does not have the facilities for examining and comparing applicants' compositions with the compositions of the prior art reference, the burden is upon applicants to show a distinction between the material structural and functional characteristics of the claimed compositions and the compositions of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594.

12. Claims 1, 3, 19-21, and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Krieg et al (WO 98/18810).

Krieg et al discloses that CpG oligonucleotides are immunostimulatory and are useful as synthetic adjuvants (abstract; p. 1; claims). Krieg et al discloses that the oligonucleotides can be used to treat, prevent or ameliorate disorders that include bacterial infection (p. 10). The infectious bacteria include *Neisseria gonorrhoeae* and *Neisseria meningitidis* (p. 17). The prior art discloses that the oligonucleotide can have a phosphorothioate bond (p. 22). "Nonspecific simulators of the immune response are known as adjuvants. The use of adjuvants is essential to induce a strong antibody response to soluble antigens (reference omitted). The overall effect of adjuvants is dramatic and their importance cannot be overemphasized. The action of an adjuvant allows much smaller doses of antigen to be used and generates antibody responses that are more persistent. The nonspecific activation of the immune response often can spell the difference

between success and failure in obtaining an immune response. Adjuvants should be used for first injections unless there is some very specific reason to avoid this.” (p. 33, l. 30-38) Krieg et al discloses the claimed SEQ ID NO: 1. “Recently an intense drive to find potent adjuvants with more acceptable side effects has led to the production of new synthetic adjuvants. The present invention provides the sequence 1826 TCCATGACGTTCTGACGTT (SEQ ID NO: 10), which is an adjuvant including CpG containing nucleic acids. The sequence is a strong immune activating sequence and is a superb adjuvant, with efficacy comparable or superior to complete Freund’s, but without apparent toxicity.” (p. 34, l. 15-20) Krieg et al discloses the use of additional adjuvants in the composition. “Immunostimulatory oligonucleotides and unmethylated CpG containing vaccines, which directly activate lymphocytes and co-stimulate an antigen-specific response, are fundamentally different from conventional adjuvants (e.g. aluminum precipitates), which are inert when injected alone and are thought to work through absorbing the antigen and thereby presenting it more effectively to immune cells. Further, conventional adjuvants only work for certain antigens, only induce an antibody (humoral) immune response (Th2), and are very poor at inducing cellular immune responses (Th1). For many pathogens, the humoral response contributes little to protection, and can even be detrimental.” (p. 65, l. 1-8)

The recitation of vaccine is viewed as intended use. The recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared

to the prior art. See *In re Casey*, 370 F.2d 576, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 312 F.2d 937, 939, 136 USPQ 458, 459 (CCPA 1963).

The prior art discloses that claimed invention. Since the Patent Office does not have the facilities for examining and comparing applicants' compositions with the compositions of the prior art reference, the burden is upon applicants to show a distinction between the material structural and functional characteristics of the claimed compositions and the compositions of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594.

13. Claims 2, 6-8, 15-18 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Krieg et al (WO 98/18810) as applied to claims 1, 3, 19-21 and 23 above, and further in view of Schwartz et al (WO 98/55495).

Krieg et al teaches that CpG oligonucleotides are immunostimulatory and are useful as synthetic adjuvants (abstract; p. 1; claims). Krieg et al teaches that the oligonucleotides can be used to treat, prevent or ameliorate disorders that include bacterial infection (p. 10). The infectious bacteria include *Neisseria gonorrhoeae* and *Neisseria meningitidis* (p. 17). The prior art teaches that the oligonucleotide can have a phosphorothioate bond (p. 22). "Nonspecific simulators of the immune response are known as adjuvants. The use of adjuvants is essential to induce a strong antibody response to soluble antigens (reference omitted). The overall effect of adjuvants is dramatic and their importance cannot be overemphasized. The action of an adjuvant allows much smaller doses of antigen to be used and generates antibody responses that are more persistent. The nonspecific activation of the immune response often can spell the difference between success and failure in obtaining an immune response. Adjuvants should

be used for first injections unless there is some very specific reason to avoid this.” (p. 33, l. 30-38) Krieg et al teaches the claimed SEQ ID NO: 1. “Recently an intense drive to find potent adjuvants with more acceptable side effects has led to the production of new synthetic adjuvants. The present invention provides the sequence 1826 TCCATGACGTTCTGACGTT (SEQ ID NO: 10), which is an adjuvant including CpG containing nucleic acids. The sequence is a strong immune activating sequence and is a superb adjuvant, with efficacy comparable or superior to complete Freund’s, but without apparent toxicity.” (p. 34, l. 15-20) Krieg et al teaches the use of additional adjuvants in the composition.

“Immunostimulatory oligonucleotides and unmethylated CpG containing vaccines, which directly activate lymphocytes and co-stimulate an antigen-specific response, are fundamentally different from conventional adjuvants (e.g. aluminum precipitates), which are inert when injected alone and are thought to work through absorbing the antigen and thereby presenting it more effectively to immune cells. Further, conventional adjuvants only work for certain antigens, only induce an antibody (humoral) immune response (Th2), and are very poor at inducing cellular immune responses (Th1). For many pathogens, the humoral response contributes little to protection, and can even be detrimental.” (p. 65, l. 1-8) Krieg et al teaches the claimed invention except for the specific additional adjuvants.

However, Schwartz et al teaches a composition comprising an immunostimulatory oligonucleotide (CpG) and antigen (abstract). Schwartz et al teaches that the antigen can be protein, glycoproteins, polysaccharides and lipids (p. 4, l. 33-34; p. 12, l. 9-28; pp. 12-13). “In another embodiment, the immunomodulatory composition comprises an oligonucleotide that contains at least one immunostimulatory (ISS) octanucleotide and a facilitator selected from

the group consisting of co-stimulatory molecules, cytokines, chemokines, targeting protein ligand, a trans-activating factor, a peptide, and a peptide comprising a modified amino acid.” (p. 4, l. 36-39; p. 12, l. 9-28) Schwartz et al teaches that the composition can also comprise the oligonucleotide, an antigen and an adjuvant (p. 5, l. 1-2; p. 8, l. 19-23). The adjuvants include alum, lipid emulsions and polylactide/polyglycolide microparticles as well as oil-in-water emulsions, mycobacterium cell wall preparations and muramyl peptide (p. 12; pp. 15-19; claims). Schwartz et al teaches that the compositions provide for methods of treating subjects in need of immune modulation; the subjects may be suffering from infectious diseases and bacterial infections (p. 5; claims). Schwartz et al teaches that the CG motif be flanked by two purines immediately 5’ to said motif and two pyrimidines immediately 3’ to said motif (p. 7, l. 14-21). Schwartz et al teaches that an immunomodulatory facilitators, molecules which support and/or enhance the immunomodulatory activity of an oligonucleotide, can be used in the composition, which include cytokines and/or adjuvants (p. 14, l. 15-36), as well as compositions comprising an oligonucleotide, antigen and adjuvant (claims).

In view of the combined teachings of Krieg et al and Schwartz et al it would have been obvious to a person of ordinary skill in the art to prepare a composition that comprises a CG oligonucleotide and a *Neisseria* antigen and optionally another adjuvant. The prior art teaches that the *Neisseria* antigen can be *Neisseria meningitidis* or *Neisseria gonorrhoeae* and an adjuvant composition comprising an oligonucleotide comprising at least one CG motif. Krieg et al teaches the claimed oligonucleotide as set forth in SEQ ID NO: 1 and teaches that it is a strong immune activating sequence and is a superb adjuvant. Both references teach the use of multiple adjuvants in the compositions. Schwartz et al teaches that the specifically

claimed additional adjuvants can be used in the compositions to enhance the immunomodulatory activity. The prior art teaches that the compositions can be used to treat infection in a subject. The claimed invention is *prima facie* obvious in view of the combination of teachings as a whole found in Krieg et al and Schwartz et al, absent any convincing evidence to the contrary.

14. Claims 2-17, 25 and 43-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Agrawal et al (WO 98/49288) as applied to claims 1, 3, 6, 7, 17-21, 23 and 24 above, and further in view of Fraser et al (WO/99/57280).

Agrawal et al discloses a composition comprising a *Neisseria* antigen and a adjuvant composition comprising an oligonucleotide comprising at least one CG motif. The prior art discloses that the compositions can be used for methods for prophylactically protect a mammal from infection by a pathogen (p. 4). Agrawal et al discloses that pathogens include *Neisseria* spp. (p. 12). Agrawal et al discloses an oligonucleotide that has at least one CG motif and it has at least one phosphorothioate bond (see p. 5; p. 10). Agrawal et al disclose that the CG motif be flanked by two purines immediately 5' to said motif and two pyrimidines immediately 3' to said motif (see p. 11). Agrawal et al disclose that the oligonucleotide should be formulated in a physiologically acceptable carrier or diluent, including without limitation saline and/or an adjuvant (pp. 8-9). Agrawal et al discloses the claimed invention except for the specific *Neisseria* protein set forth in claimed SEQ ID NO: 31.

However, Fraser et al teaches antigens of *Neisseria meningitidis* serogroup B and *Neisseria gonorrhoeae* as well as amino acid sequences to the antigens and that they can be used in compositions (p. 4-5; p. 7; p. 134; p. 8). Claimed SEQ ID

NO: 31 is found on p 134 of Fraser et al (also see attached sequence search printout). Fraser et al teaches that the compositions can comprise adjuvants and other components that promote or enhance the antigen (pp. 32-33; p. 34). Fraser et al disclose oil droplets as well as adjuvants such as aluminum salts, oil-in-water emulsion formulations that contains 5% squalene or 10% (i.e. oil) and 0.5% or 0.4% Tween 80 (i.e. emulsifying agent), saponin adjuvants, complete Freund's adjuvant, incomplete Freund's adjuvant and muramyl peptides (pp. 35-36).

In view of the combined teachings of Agrawal et al and Fraser et al it would have been obvious to a person of ordinary skill in the art to prepare a composition comprising a *Neisseria* antigen (*Neisseria meningitidis* serogroup B and *Neisseria gonorrhoeae*) and an adjuvant composition comprising an oligonucleotide comprising at least one CG motif. Agrawal et al teaches the claimed oligonucleotide as set forth in SEQ ID NO: 1 and teaches that it has adjuvant or immunostimulating properties as well as the fact that Agrawal et al teaches treating bacterial infections and disease. Both references teach the use of multiple adjuvants in the compositions. Fraser et al teaches the specific antigen of *Neisseria* claimed by Applicants set forth in SEQ ID NO: 31 and teaches that all of these antigens can be used in vaccine, pharmaceutical and therapeutic compositions. The claimed invention is prima facie obvious in view of the combination of teachings as a whole found in Agrawal et al and Fraser et al, absent any convincing evidence to the contrary.

15. Claims 1-3, 6-8, 15, 17-21, 23 and 24 are rejected under 35 U.S.C. 102(e) as being anticipated by Friede et al (6558670).



Fried et al discloses a composition that comprises an antigen and an adjuvant (an immunostimulatory oligonucleotide) as well as the use of combination adjuvants (abstract; col. 3). Friede et al discloses that the immunostimulatory oligonucleotide comprises the following sequence: Purine, Purine, C, G, Pyrimidine, Pyrimidine (col. 2). Friede et al discloses that the adjuvant compositions can be used in vaccine compositions (col. 3). Friede et al discloses the claimed oligonucleotide sequence, SEQ ID NO: 1 (see col. 3, l. 55-56; sequence listing-SEQ ID NO: 1). Friede et al discloses that the vaccine formulations can contain an antigen or antigenic composition capable of eliciting an immune response against a human pathogen, and that the antigen could be derived from proteins from bacterial pathogens such as *Neisseria* spp., *Neisseria meningitidis* and *Neisseria gonorrhoeae* (col. 5). Friede et al discloses the use of other antigens such as aluminum hydroxide, oil-in-water emulsions, aluminum salts (col. 9).

The prior art discloses that claimed invention. Since the Patent Office does not have the facilities for examining and comparing applicants' compositions with the compositions of the prior art reference, the burden is upon applicants to show a distinction between the material structural and functional characteristics of the claimed compositions and the compositions of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

16. No claims are allowed.

17. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read 'N. M. Minnifield', is written over a printed name.

N. M. Minnifield  
Primary Examiner

Art Unit 1645

NMM

April 19, 2005

Application/Control Number: 09/914,454  
Art Unit: 1645

Page 18

PLEASE MAIL WITH  
OFFICE ACTION 4-20-05  
Page 2

CC for inducing a protective immune response in a mammal. The present  
CC sequence represents the Memb 919 protein, which is used in an example  
XX from the present invention  
SQ Sequence 441 AA;

Query Match 100.0%; Score 2340; DB 4; Length 441;  
Best Local Similarity 100.0%; Pred. No. 1.2e-222;  
Matches 441; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MKKYLFRALYGIATAIILAAACOSKSIOTFPQDPTSVINGEDRPVGIIPDPAGTTVGGGAV 60  
DB 1 MKKYLFRALYGIATAIILAAACOSKSIOTFPQDPTSVINGEDRPVGIIPDPAGTTVGGGAV 60  
QY 61 YTVVPHLSLPHMAADPAKSLQSFRLGCAVILKRRQGMQDVCAQAFOTPVHSPQAKOFFER 120  
DB 61 YTVVPHLSLPHMAADPAKSLQSFRLGCAVILKRRQGMQDVCAQAFOTPVHSPQAKOFFER 120  
QY 121 YTFPMQVANGSLAGTGTGTYEPEVLKGDRTTAQARFPYIGIPDDEISVPLPAGLSGKA 180  
DB 121 YTFPMQVANGSLAGTGTGTYEPEVLKGDRTTAQARFPYIGIPDDEISVPLPAGLSGKA 180  
QY 181 LVRIROTKNSGTDINTGTHADLSRPTTATTAIKRFGSGRLPYHTNQINGAL 240  
DB 181 LVRIROTKNSGTDINTGTHADLSRPTTATTAIKRFGSGRLPYHTNQINGAL 240  
QY 241 DGRAPILGYAEDPVELFPMHIOGSGRLKTPSGKYIRIGYADKNEHPYVSIGRYMDKGL 300  
DB 241 DGRAPILGYAEDPVELFPMHIOGSGRLKTPSGKYIRIGYADKNEHPYVSIGRYMDKGL 300  
QY 301 KLGSOTSMGISKYMNQORLAELVGNPSYIFFRELASSNDGVPVGLGTPLMGEYAGA 360  
DB 301 KLGSOTSMGISKYMNQORLAELVGNPSYIFFRELASSNDGVPVGLGTPLMGEYAGA 360  
QY 361 VDRHYITIGAPLFAVATAPVTRKALNRLIMADGTSALIDGAVRVDFYWGDEAGELAGK 420  
DB 361 VDRHYITIGAPLFAVATAPVTRKALNRLIMADGTSALIDGAVRVDFYWGDEAGELAGK 420  
QY 421 OKTTGYVWQLLPNGMKPEYRP 441  
DB 421 OKTTGYVWQLLPNGMKPEYRP 441

RESULT 2  
AAV75911  
AAV75911 standard; protein; 441 AA;  
AAV75911;

DT 21-MAR-2000 (first entry)  
XX Neisseria strain zmo3 ORF 919 protein SEQ ID NO:3211.

XX Neisseria meningitidis; Neisseria gonorrhoeae; antigen; vaccine;  
KW anti-genic; diagnosis; immunogenic; infection; meningitis; septicemia;  
XX anti-bacterial; gene therapy.

OS Neisseria sp.

XX MO9957280-A2.

PD 11-NOV-1999.

XX 30-APR-1999; 99MO-US009346

XX 01-MAY-1998; 98US-0083758P

PR 31-JUL-1998; 98US-0094869P

PR 02-SEP-1998; 98US-0098944P

PR 02-SEP-1998; 98US-0099062P

PR 09-OCT-1998; 98US-0103749P

PR 09-OCT-1998; 98US-0103794P

PR 25-FEB-1999; 98US-0103796P

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XX (CHIR) CHIRON CORP.  
PA (GENO-) INST GENOMIC RES.  
PI Fraser C, Galeotti C, Grandi G, Hickey E, Masignani V, Mora M,  
PI Petersen U, Pizzo M, Rappelli R, Ratti G, Scalato E, Scarselli M,  
PI Tettein H, Venter JC,  
XX WPI; 2000-062150/05.

Novel Neisserial polypeptides predicted to be useful antigens for  
vaccines and diagnostics.

Example 15; Page 134; 1453pp; English.

AAZ53015 to AAZ54536, AAZ54577 to AAZ54615, and AAV74253 to AAV75941  
represent novel Neisseria meningitidis and N. gonorrhoeae polynucleotides  
and polypeptides. AAZ54537 to AAZ54576 and AAZ54616 to AAZ5473 represent  
PCR primers used in the exemplification of the present invention. The  
polypeptides, the polynucleotides, antibodies and compositions of the  
invention can be used as vaccines, as diagnostic reagents, and as  
immunogenic compositions. The polypeptides can be used in the manufacture  
of medicaments for treating or preventing infection due to Neisseria  
bacteria (e.g. meningitis and septicemia), to detect the presence of  
Neisseria bacteria, or to raise antibodies. They may also be used to  
screen for agonists or antagonists, which may themselves have use as  
antibacterial agents. The polynucleotides of the invention may also be  
used in gene therapy protocols

SQ Sequence 441 AA;

Query Match 99.7%; Score 2333; DB 3; Length 441;  
Best Local Similarity 99.8%; Pred. No. 6.1e-222;  
Matches 440; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

QY 1 MKKYLFRALYGIATAIILAAACOSKSIOTFPQDPTSVINGEDRPVGIIPDPAGTTVGGGAV 60  
DB 1 MKKYLFRALYGIATAIILAAACOSKSIOTFPQDPTSVINGEDRPVGIIPDPAGTTVGGGAV 60  
QY 61 YTVVPHLSLPHMAADPAKSLQSFRLGCAVILKRRQGMQDVCAQAFOTPVHSPQAKOFFER 120  
DB 61 YTVVPHLSLPHMAADPAKSLQSFRLGCAVILKRRQGMQDVCAQAFOTPVHSPQAKOFFER 120  
QY 121 YTFPMQVANGSLAGTGTGTYEPEVLKGDRTTAQARFPYIGIPDDEISVPLPAGLSGKA 180  
DB 121 YTFPMQVANGSLAGTGTGTYEPEVLKGDRTTAQARFPYIGIPDDEISVPLPAGLSGKA 180  
QY 181 LVRIROTKNSGTDINTGTHADLSRPTTATTAIKRFGSGRLPYHTNQINGAL 240  
DB 181 LVRIROTKNSGTDINTGTHADLSRPTTATTAIKRFGSGRLPYHTNQINGAL 240  
QY 241 DGRAPILGYAEDPVELFPMHIOGSGRLKTPSGKYIRIGYADKNEHPYVSIGRYMDKGL 300  
DB 241 DGRAPILGYAEDPVELFPMHIOGSGRLKTPSGKYIRIGYADKNEHPYVSIGRYMDKGL 300  
QY 301 KLGSOTSMGISKYMNQORLAELVGNPSYIFFRELASSNDGVPVGLGTPLMGEYAGA 360  
DB 301 KLGSOTSMGISKYMNQORLAELVGNPSYIFFRELASSNDGVPVGLGTPLMGEYAGA 360  
QY 361 VDRHYITIGAPLFAVATAPVTRKALNRLIMADGTSALIDGAVRVDFYWGDEAGELAGK 420  
DB 361 VDRHYITIGAPLFAVATAPVTRKALNRLIMADGTSALIDGAVRVDFYWGDEAGELAGK 420  
QY 421 OKTTGYVWQLLPNGMKPEYRP 441  
DB 421 OKTTGYVWQLLPNGMKPEYRP 441

RESULT 3  
AAV75920  
ID AAV75920 standard; protein; 441 AA.  
AC AAV75920;